Evaluation of Biodentine™ in the restoration of root caries: a randomized controlled trial

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Clinical evaluation of Biodentine™ in the restoration of root caries lesions in older adults- a randomised controlled trial

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1. Introduction

The world population is rapidly ageing. Between 2000 and 2050, the proportion of the world's population over 60 years will double from about 11% to 22%. The absolute number of people aged 60 years and over is expected to increase from 605 million to 2 billion over the same period (United Nations Department of Economic and Social Affairs, 2002). Alongside this trend in global ageing there is a concomitant reduction in levels of edentulism in developed countries (Chen et al., 1997, Control and Prevention, 2003, Health and Services, 2014, Petersen et al., 2004). As a result we can expect to see an increase in the prevalence of root caries as it has been shown that older people are at a higher risk of root caries than younger populations due to an increased number of exposed root surfaces (Chi et al., 2013, Fejerskov et al., 1991).

Restoration of these lesions is challenging as the cavities are broad and saucer shaped with ill-defined margins which can be positioned in enamel as well as dentine (Wefel et al., 1985). A systematic review looking at the operative management of root caries lesions identified only five clinical trials in the literature (Hayes et al., 2014). Most of the studies had less than 50 participants and recruited individuals who had xerostomia secondary to radiation treatment which may not be representative of most of the population with root caries. Failure rates were high across all restorative materials and at present there is no ‘gold-standard’ material for this indication.

In 2011, Biodentine™ was developed as a dentine replacement material by Septodont. This quick-setting calcium silicate based dental cement is novel as it may be placed as a coronal restoration as well as used for endodontic procedures. Biodentine has many favourable biological properties and encourages dentine bridge formation with no inflammatory pulp response through secretion of TGF-ß1 (Laurent and Camps, 2012, Nowicka et al., 2013). A recent clinical trial reported very promising results when Biodentine™ was placed as an indirect pulp cap in deep carious lesions in teeth with clinical signs of reversible pulpitis (Hashem et al., 2015).

As root carious lesions are often confined to dentine, and this material produces mineral tags in dentinal tubules, Biodentine™ has the potential to offer high micro-leakage resistance (Han and Okiji, 2011). When this material was introduced to the market it was described as having “similar mechanical properties and mechanical behaviour as human dentin” and a clinical trial subsequently concluded that Biodentine™ could be successfully used as a posterior restoration material for up to six months (Koubi et al., 2012). However, review articles published to date have unanimously concluded that a lack of clinical outcome data precludes a definitive conclusion about this novel material (Rajasekharan et al., 2014, Chen and Jorden, 2010, Meshack et al., 2012, Bogen and Chandler, 2012, Malkondu et al., 2014).

The aim of this study was to determine if the clinical performance of Biodentine would be acceptable for the restoration of root caries lesions in older adults. As mentioned there is currently no standard material for this use to compare it to, however studies to date have assessed glass ionomer cement, resin modified glass ionomer cement, resin composite and amalgam. As much controversy surrounds the use of dental amalgam due to its mercury content, it is unlikely that we can consider amalgam a viable long term restorative material. Resin composite could not be used as a control in this study as many root caries lesions extend subgingivally and isolation would not be possible to allow predictable dentine bonding. Therefore both a conventional glass ionomer cement (GIC) (Fuji IX GP® Extra, GC Corporation) and a resin-modified glass ionomer cement (RMGIC) (Fuji II LC®, GC Corporation) were chosen as controls. Previous clinical studies have shown that both of these materials have similar survival rates in root caries lesions (Lo et al., 2006, da Mata et al., 2015). The null hypothesis of this study stated that the six-month and one-year survival of Biodentine™ restorations would be no worse than that of either Fuji IX GP® Extra or Fuji II LC® when used to restore root caries in older individuals. This randomized controlled clinical trial was conducted following the CONSORT guidelines.

2. Methods

2.1 Study Design

A 3-arm randomised controlled clinical trial (ClinicalTrials.gov Identifier: NCT01866059) was conducted comparing Biodentine™ as the test material and GIC (Fuji IX GP® Extra, GP Corporation) and RMGIC (Fuji II LC®, GC Corporation) as the two control groups. As in similar studies, the study was not operator blinded because of the different appearance of the materials and the different operative procedures in their placement. The study protocol was submitted and given full ethical approval by the Clinical Ethics Committee of the Cork Teaching Hospitals (ECM 4 Y 06/12/11). The study was conducted in compliance with the principles of the Declaration of Helsinki and written informed consent was obtained from each participant.

2.2 Recruitment

Adults aged over 65 years of age with any of their remaining natural dentition were invited to attend Cork University Dental School and Hospital for a free dental examination. Advertisements were placed in local shopping centres, community centres and the local press. Contact details of the study coordinator were provided and patients were allocated appointments. All of the patients recruited to the study were independently living older adults. No financial rewards were offered to patients but all treatment costs involved in the study were covered.

2.3 Clinical examination

Upon entering the study each patient completed a patient questionnaire and received a clinical examination. The examination comprised a hard tissue charting with separate examination of the coronal tooth structure and the

root, visible plaque index, a basic periodontal examination (BPE), and removable partial denture contacts. Hard tissue charting was recorded following removal of plaque and calculus deposits. A surface was categorised as in close contact with a partial denture if it was within 3mm of any denture component. Patients who fulfilled the inclusion criteria for the study were invited to participate and given a unique identifier.

2.4 Inclusion and exclusion criteria

The inclusion criteria for entering this study were:

- Be aged 65 or over
- Present a minimum of 2 teeth with active cavitated root caries lesions
- Have sufficient cognitive ability to understand consent procedures

The exclusion criteria for this study were:

- Medically frail individuals (ASA IV)
- Individuals presenting with any painful symptomology other than sensitivity
- Individuals with severe periodontal disease
- Individuals requiring antibiotic prophylaxis for invasive dental treatment

2.5 Randomisation

A computer generated randomisation scheme was generated using Microsoft® Office Excel® software for the eight strata arising from the stratification variables: denture wearing (yes/no); dry mouth (yes/no); number of root caries i.e. treated plus untreated (2 ,3 , 4 or more). The unit of randomisation was the tooth. Randomisation was conducted by a research assistant and the allocation was concealed from the clinical operator until the time of restoration placement.

2.6 Power calculation

A sample size calculation was performed in order to demonstrate non-inferiority of Biodentine™ survival rate relative to conventional treatment (GIC and RMGIC) at one year. The survival of the conventional treatments was estimated to be 85% based on previous studies (De Moor et al., 2011, Lo et al., 2006, McComb et al., 2002). GIC and RMGIC would be applied in a ratio of 1:1 in the control group. In determining the sample size, we regarded a difference in restoration survival rate of 15% or more as clinically significant. Using an 80% power and a 5% statistical significance level, we found that 71 restorations per group would be necessary (i.e. 71 Biodentine™ and 71 control). In anticipation of a 15% drop-out rate, this was increased to 82. The sample size was then increased by a factor of 1.5 in an attempt to correct for lack of independence. Therefore a total of 123 restorations per group was necessary at baseline with an achieved sample of 105 per group at one year required for adequate power.

2.7 Data collection

Each participant completed a questionnaire which recorded age, gender, medical history including medications, fluoride exposure, oral and denture hygiene practices, smoking and alcohol consumption, diet information, self-reported oral dryness and socio economic information. Clinical examinations were performed and the data was entered into case report forms. Stimulated saliva samples were taken at a separate appointment as patients has to be advised to avoid eating, drinking, smoking, chewing gum, tooth brushing or mouthwashes for one hour prior to sample collection. Saliva was collected over a period of five minutes following one minute of stimulation by having the participant chew a paraffin pellet. Xerostomia was defined as < 0.7 ml saliva/min.

2.8 Operative care

All of the operative caries management was completed by a single operator. Local anaesthesia was provided if the patient requested it or if the operator felt it would be necessary. Cavity preparation was carried out with low speed rotary instruments and hand instruments for the removal of soft carious tissue. Following the principles of modern, minimally invasive caries removal(Banerjee and Watson, 2011), only caries infected dentine was removed. Caries affected dentine was not removed unless needed for cavity margin seal. Moisture control was achieved with the use of cotton wool rolls and a saliva ejector. Cavities receiving either of the control materials (GIC or RMGIC) were conditioned with a polyacrylic acid (GC Dentin conditioner, GC Corporation) for 20 seconds. Both the GIC and RMGIC used were encapsulated versions. In the case of RMGIC the material was light-cured for 20s.

For the Biodentine™ group cavities were not conditioned. In accordance with the manufacturer's instructions five drops of liquid were added to the powder single unit. All mixing was completed by one research assistant who was provided with training by Septodont. After mixing 30 s at 4,000-4,200 rpm, the Biodentine™ was applied and allowed to set untouched for 12 min. The final restorations in all groups were then coated with a varnish (G-coat plus, GC Corporation).

2.9 Evaluation of restorations

Patients were reviewed 6 months and one year after the restorations had been placed by a calibrated dentist who was not involved in restoration placement and who was blinded to material allocation. Restorations were assessed according to a modified USPHS criteria (Table 1). In this study failure was defined as loss of the restoration, fracture of the restoration exposing the base of the cavity, the presence of recurrent caries,

replacement of the restoration with another restoration, patient experiencing pain in the tooth, or loss of the tooth.

2.10 Statistical analysis

All data were entered into IBM SPSS (Version 22). Cumulative survival proportions at six months and one year were defined as the number of restorations still in situ or with acceptable marginal defects or wear at that time point, divided by the total number of restorations assessed in that group.

A logistic regression model with survival of the restoration at 12 months as the outcome variable was fitted. The explanatory variables included were: age, gender, restorative material, restoration location (root surface), proximity of restoration to gingival margin (supra-gingival or within 1mm of gingival margin/subgingival) tooth location (anterior or posterior), xerostomia, and partial denture contact.

Individual restorations could not be assumed to be independent as each participant received at least two restorations and the usual method of calculating the standard errors of the logistic regression parameters could not be used. Thus, these parameters were estimated based on 5000 Bootstrap samples from 81 participants. The tests of significance of the logistic regression parameters were based on these Bootstrap estimates of the standard errors.

3. Results

The consort flow diagram is illustrated in Figure 1. In total, 334 adults attended for examination after receiving information about the study. Of these, 251 were excluded. 249 did not fulfil the criteria. Upon receiving further information about the treatment randomisation in the study two individuals declined to participate and were excluded from the study. 85 individuals with 305 root caries lesions participated in the study. 151 lesions were assigned to receive Biodentine™, 77 lesions were allocated to Fuji IX GP® Extra, and 77 were restored with Fuji II LC®. Of the 85 participants,

one patient was lost to follow up at six months and four were lost to follow up at one year. Two of these patients were unwell and a further two could not be contacted by telephone and did not respond to letters sent to their addresses. Therefore 303 restorations in 84 participants were assessed at 6 months post-treatment and 291 restorations in 81 participants were assessed at one year post-treatment.

Table 2 illustrates the baseline demographics of the study participants and Table 3 describes the characteristics of each cavity that was restored. 54 male participants and 31 female participants with a mean age of 71.9 (SD: 4.9) were included in this study. The majority of participants (35%) received two restorations and 78% of participants received 4 restorations or less. Most of the cavities restored were confined to one root surface (74.1%) and were located on the buccal (41%) or interproximal surfaces (45.3%). 78.7% of cavities were within 1mm of the gingival margin or subgingival.

At six months, 88 (58%) of Biodentine™ restorations were assessed as being clinically acceptable and at one year, 68 (48%) of Biodentine™ restorations were clinically acceptable. Of the 74 restorations that failed over the twelve month period, 11 had developed recurrent caries and 63 were completely or partly missing. Most failures occurred within the first six months of placement. Of the Fuji IX GP® Extra restorations, 90% were clinically acceptable at six months and 85% were clinically acceptable at one year. Of the 15 restorations that failed within the year, 4 were due to recurrent caries, ten were completely or partly missing and one was due to loss of the tooth. 89% of Fuji II LC® restorations were clinically acceptable at six months and this had fallen to 84% at one year. 16 restorations in total failed within 12 months of placement and 4 of these were due to recurrent caries. The remaining 12 were completely or partly missing.

Table 5 reports the results of the logistic regression model. Of the variables examined, Biodentine™ restorative material, xerostomia and close proximity to the gingival margin/ extension of the cavity subgingivally were all found to be statistically significantly associated with an increased risk of restoration failure. Restorations placed on the distal root surface were found

to have increased odds of success at one year compared to those placed on the buccal root surface.

4. Discussion

There is a scarcity of data regarding the performance of different restorative materials for the operative treatment of root caries. In particular the majority of the data available relates to profoundly xerostomic patients post-radiotherapy to the head and neck. This study represents one of a small number which recruited independently living older adults; a population group which form an increasing proportion of the patients treated in general dental practice.

Unusually for dental research, more men than women participated in this study. While approximately equal numbers of males and females were assessed for eligibility, women tended to have more treated root caries lesions i.e. more restorations on their root surfaces, while men tended to have more active cavitated lesions and were therefore eligible for participation in this research. 15% of participants displayed hypo-salivation as measured by timed collection of stimulated saliva. This proportion is not surprising as a recent meta-analysis comparing the salivary flow rates of younger and older adults found that the ageing process is associated with reduced salivary flow even in non-medicated individuals (Affoo et al., 2015). Over half of participants (55.3%) wore removable dental prosthesis which is a recognised risk factor for root caries (Ritter et al., 2010). The mean DMFT of the group was 24.7 which is similar to that reported for this age group in our most recent national oral health survey (Whelton et al., 2007).

There was a statistically significant higher rate of failure of Biodentine™ restorations compared to the Fuji Ix GP® Extra or Fuji II LC®. As the operator placing the restorations would have had more clinical experience in handling glass ionomer cement and resin modified cement there was concern that operator technique may have increased the failure rate of the material. However an analysis comparing the survival of the first 40 Biodentine™ restorations to the final 40 did not show any statistically significant difference between the two groups, thus discounting the

hypothesis that the failures could be attributed to an operator “learning curve”.

Encapsulated versions of the glass ionomer cement and resin modified glass ionomer cement were used in this study and so the powder/liquid ration of these materials and the handling characteristics were consistent. Despite following the manufacturer’s instructions (i.e. adding five drops of liquid to the powder in the capsule) there was more variability in the consistency of the Biodentine™ and this may be a factor in the survival of these restorations. It is also important to note that the setting time of Biodentine® is twelve minutes which is much longer than that of Fuji IX GP® Extra (2.5 mins) or Fuji II LC® (command set in 20sec). This longer setting time allows a wider window of opportunity for moisture contamination during the initial set which would weaken the final cement.

In all materials the risk of failure was higher when placed in a cavity which was in close proximity to the gingival margin (within 1mm) or extended subgingivally. 79% of cavities restored in this study were located in this area and would have been subject to the dynamic flow of gingival crevicular fluid (GCF). This may be detrimental to Biodentine™ restorations which demonstrate a high level of washout (Grech et al., 2013). This tendency of the freshly prepared cement to disintegrate upon early contact with blood or saliva is a fundamental drawback when placing this material subgingivally.

As is the nature of carious lesions on root surfaces, many of the cavities were broad and shallow in form. Box-form cavities were not prepared and conservative caries removal dictated cavity design. As a result many of the restorations placed were thin in section. It is probable that the majority of the restorations placed in this clinical trial were shallower than those in the trial reported by Koubi et al. We are not aware if there is a minimum bulk recommended for Biodentine™ restorations. Also large areas of the cavity floor of these cavities was composed of caries-affected dentine, therefore the bonding substrate was caries-affected dentine rather than normal cut dentine. In the package inset, the manufacturers of Biodentine™ recommend that as much decay as possible should be removed from the cavity. An in-vitro study is currently running to assess if and how much carious tissue can be left.

A combination of all the factors discussed above may account for the higher failure rates reported in this trial than the previously published clinical trial (Koubi et al., 2012).

5. Conclusions

Based on the results of this study, Biodentine™ cannot be recommended for the restoration of root caries in older adults. Fuji IX GP® Extra and Fuji II LC® displayed similar success rates and glass ionomer cement and resin modified class ionomer cement continue to be the best available option for the operative treatment of root caries.

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Table 1. Modified USPHS Criteria for Restoration Assessment

Criterion	Status	Code
Retention	Yes	0
	No	1
Marginal integrity	No crevice	0
	Crevice, no dentine exposed	1
	Defect extended to ADJ	2
	Restoration fractured or missing	3
Marginal discolouration	No discolouration	0
	Discolouration, no penetration	1
	Discolouration with penetration	2
Recurrent caries	No	0
	Yes	1
Anatomic form	Continuous with anatomy	0
	Discontinuous	1
Surface texture	Similar to polished enamel	0
	Gritty, similar to white stone	1
Patient's view	Entirely satisfied	0
	Satisfied	1
	Minor criticism of aesthetics	2
	Aesthetics acceptable	3
	Experiencing pain	4

Figure 1. CONSORT Flow Diagram

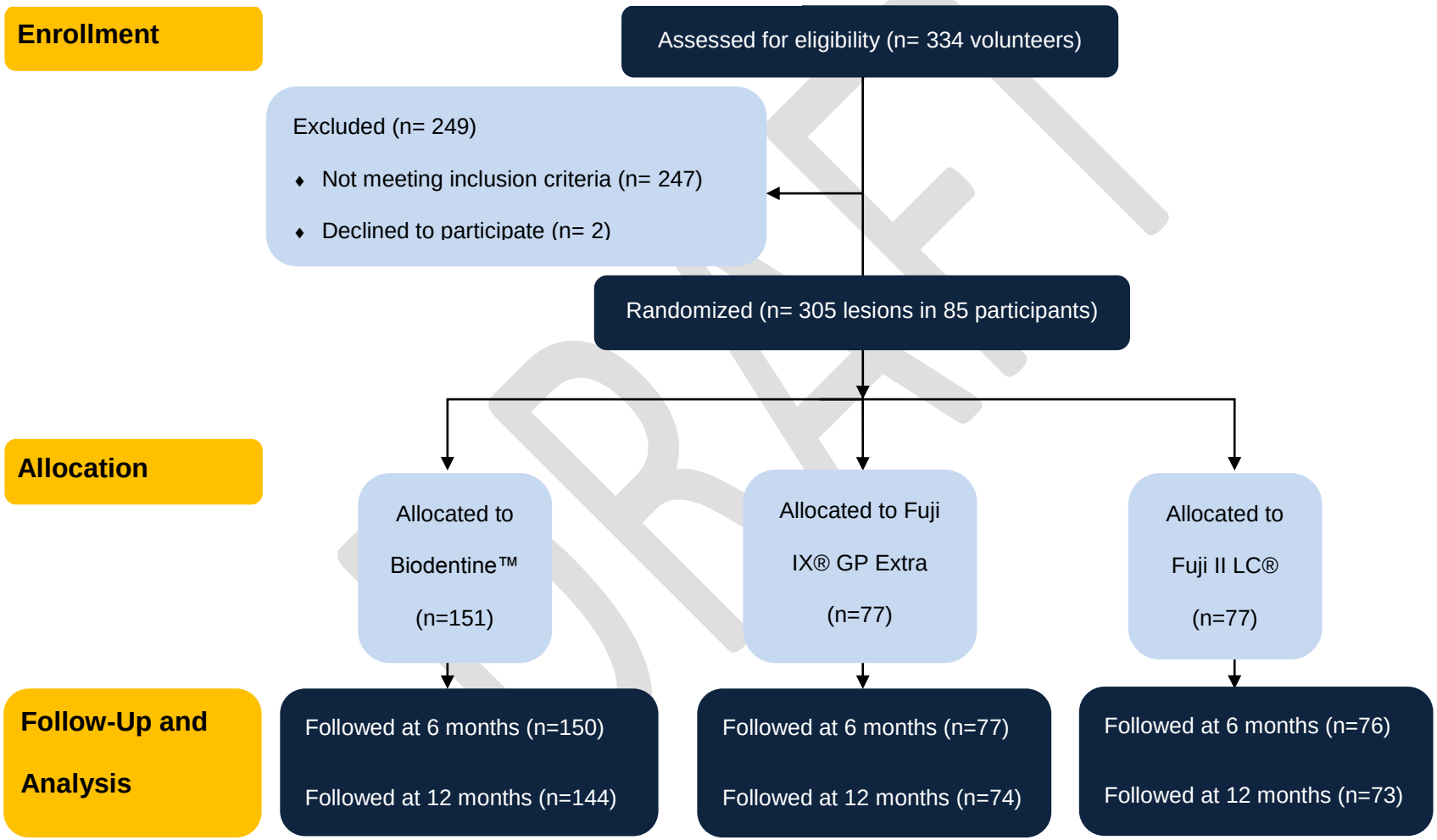

Table 2. Patient Characteristics	n=85
Gender	
Male	54 (63.5%)
Female	31 (36.5%)
Age	
Mean (SD)	71.9 (4.9)
Range	65-83
Root Caries Index	
Mean (SD)	24.7 (17.7)
Range	2.5-93.8
Decayed Missing Filled Teeth (DMFT)	
Mean (SD)	24.5 (4.8)
Range	14-32
Denture wearing	
Yes	47 (55.3%)
No	38 (44.7%)
Xerostomic	
Yes	13 (15.3%)
No	72 (84.7%)
ASA category	
ASA 1	26 (30.6%)
ASA 2	41 (48.2%)
ASA 3	18 (21.2%)
Smoking status	
Smoker	20 (23.5%)
Past smoker	21 (24.7%)
Never smoked	44 (51.8%)
Dental attendance	
Regular attender	41 (48.2%)
Irregular attender	44 (51.8%)

Table 3. Cavity/Restoration Level Data	n=305
Material placed	
Biodentine™	151 (49.5%)
Fuji IX GP® Extra	77 (25.2%)
Fuji II LC®	22 (25.2%)
Xerostomic mouth	
Yes	64 (21.0%)
No	241 (79.0%)
Removable partial denture contact	
Yes	109 (35.7%)
No	196 (64.3%)
Tooth type	
Upper	167 (54.8%)
Lower	138 (45.2%)
Anterior (Incisor or canine)	143 (46.9%)
Posterior (Premolar or molar)	162 (53.1%)
Number of surfaces involved	
1 surface	226 (74.1%)
2 surfaces	67 (22.0%)
3 surfaces	12 (3.9%)
Proximity to gingival margin	
Within 1mm gingival margin/subgingival	240 (78.7%)
Supra-gingival	65 (21.3%)
Location of restoration	
Buccal	125 (41.0%)
Lingual	30 (9.8%)
Palatal	12 (3.9%)
Mesial	74 (24.3%)
Distal	64 (21.0%)

Table 4. Survival at 6 months and one year				
	Six months		One year	
	Yes (%)	No (%)	Yes (%)	No (%)
Biodentine™	88 (58)	62 (41)	68 (48)	74 (52)
Fuji IX GP® Extra	69 (90)	8 (10)	61 (85)	11 (15)
Fuji II LC®	68 (89)	8 (10)	60 (84)	11 (16)
Total	225 (74)	78 (26)	189 (66)	96 (34)

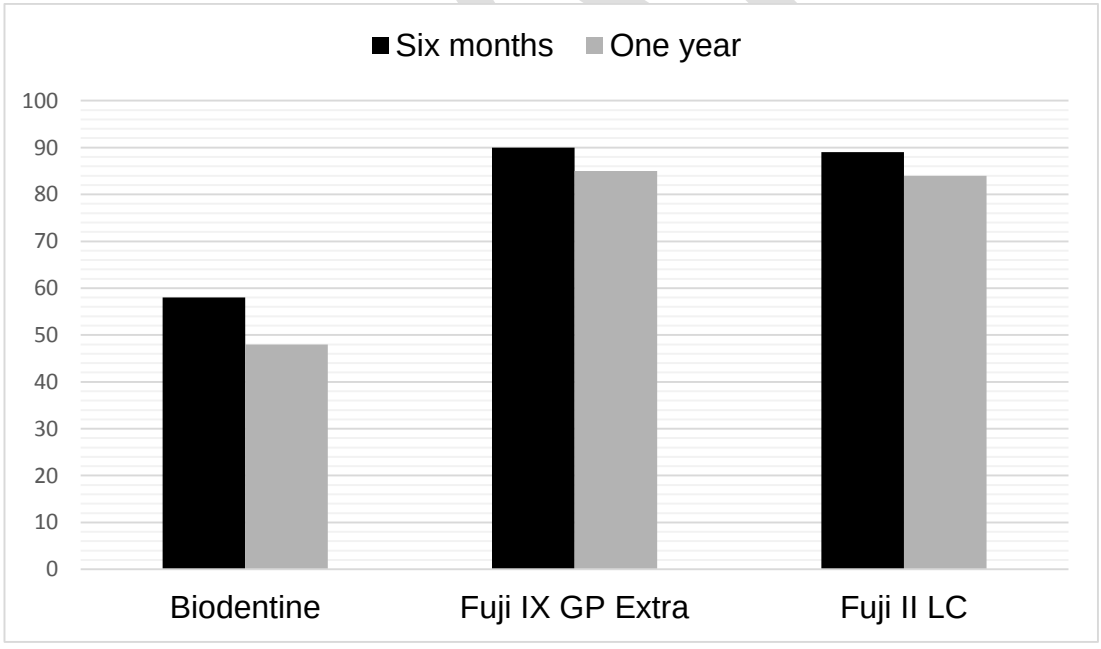

Figure 2. Cumulative survival proportions at six months and one year

Table 5. Odds ratio (OR) and 90% confidence intervals (90%CI) for survival of restorations

Variable	Odds ratio	90% CI		*p* - value
Xerostomia				
No				
Yes	0.18*	0.08*	0.44*	0.002*
Denture Abutment				
No				
Yes	2.08	0.97	4.46	0.11
Caries experience				
RDFS ≤ 5 at Baseline				
RDFS >5 at Baseline	0.96	0.44	2.05	0.93
Root Surface Restored				
Buccal				
Lingual	1.35	0.44	4.06	0.67
Palatal	1.34	0.25	7.31	0.77
Mesial	0.97	0.49	1.89	0.94
Distal	5.63*	2.38*	13.29*	0.001*
Age				
<75				
≥75	0.90	0.36	0.47	1.89
Gender				
Male				
Female	0.63	0.9	0.31	1.27
Restorative Material				
Fuji IX/Fuji II®				
Biodentine™	0.11*	0.06*	0.21*	0.001*
Restoration Location				
Within 1mm gingival margin/sub-gingival				
Supra-gingival	2.68*	1.28*	5.59*	0.03*
Tooth Type				
Anterior/Premolar				
Molar	0.83	0.47	0.47	1.49

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